Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

This amendment is accompanied by the requisite RCE fees and extension of time fees. Because the deadline for response fell on Saturday September 2, 2006 (as calculated from the date of entry for the previously submitted Notice of Appeal), this submission is timely filed.

By this amendment, claim 7 has been amended, claims 8, 82, 87, and 90 (previously identified as allowable) have been cancelled, and new claims 91-98 have been introduced. New claim 91 presents a Markush group listing the subject matter of previously presented claims 8, 87, and 90, now in independent form. The subject matter of claims 8, 87, and 90 appears in new claims 92-94, respectively; and the subject matter of claim 82 appears in new claim 95. New claims 96-98 find descriptive support in original claims 22, 28, and 29. No new matter has been introduced.

The objection to claims 8, 82, 87, and 90 is overcome by the above amendments.

The rejection of claims 7, 22, 28, 29, 81, 83-86, 88, and 89 under 35 U.S.C. § 112 (1st para.) as lacking written descriptive support is respectfully traversed.

The specification identifies the polynucleotides of SEQ ID NOS: 1 and 3 as *dnaX* polynucleotides of *Thermus thermophilus*. These two sequences are related in that SEQ ID NO: 3 is the coding sequence contained within SEQ ID NO: 1. Applicants submit that the recitation of these sequences in Figures 4A-B and 4C, the identification of ATP-binding (GXXGXGKT) and Zn^{2+} finger consensus sites among tau/gamma subunits conserved among both *Thermus thermophilus* and distantly related bacteria in Figure 5 (*see also* Example 8, at pages 71-75), and the demonstration of ATPase activity of the tau/gamma subunits (*see* Example 7, first occurrence, at pages 69-71) confirm that applicants were in possession of the claimed product. Given the above data provided by applicants, persons of skill in the art would have expected other members of the *Thermus* genus to possess a similar structure and function to that demonstrated for the *dnaX* of SEQ ID NOS: 1, 3 and tau/gamma subunits of SEQ ID NOS: 2, 4, and 5.

Applicants submit that the evidence previously presented (with the May 11, 2005, amendment) and presented as attached Exhibits A-C demonstrate that the species of SEQ ID NOS: 1 and 3 adequately represent the claimed subject matter.

As described in the amendment dated May 11, 2005, McHenry et al., "A DNA Polymerase III Holoenzyme-like Subassembly from an Extreme Thermophilic Eubacterium," *J. Mol. Biol.* 272:178-189 (1997) ("McHenry") identifies the 63 and 50 kDa protein products of the *T. thermophilus dna*X gene as the γ and τ subunits of *T. thermophilus*. The *dnaX* gene of McHenry shares 98% homology with the nucleotide sequence of SEQ ID NO: 1 (and, thus, SEQ ID NO: 3), and the corresponding tau and gamma subunits share 98% and 97% homology, respectively, with those identified in the present application. In addition to this evidence, attached hereto as Exhibit A are Genbank Accessions NC_006461 (submission by Masui et al.) and AE017221 (submission by Henne et al.), which identify the coding sequence and encoded tau products for *Thermus thermophilus* strains HB8 and HB27, respectively. These *dnaX* nucleic acids were identified by a protein-protein BLAST search of the Genbank database performed using the amino acid sequence of SEQ ID NO: 2 and the BLAST default settings. Based upon alignments performed using Align® for nucleic acids and ClustalW for amino acids (using the European Molecular Biology Laboratory server and its default settings), the Masui et al. and Henne et al. *dnaX* homologs both share about 99 percent identity to SEQ ID NO: 3 at the nucleic acid level (Exhibit B) and about 98 percent homology to SEQ ID NO: 2 at the amino acid level (Exhibit C). Both the Henne et al. and Masui et al. tau/gamma sequences possess the ATP consensus and Zn^{2+} finger domains identified in the specification (*compare* first and second rows in the alignments at Exhibit C, showing complete identity of GPRGVGKT residues 43-50 and Cys residues 62, 69, 72, and 75). Thus, species of *dnaX* (encoding tau/gamma subunits) from thermophilic organisms that belong to the biological classification *Thermus* clearly share similar structure and, therefore, function.

Applicants submit that the language recited in claim 7 is precisely the type of claim language that was acknowledged in *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) as being acceptable under the written description requirement. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. ("Rutter"), specifically those claims that recited the limitations 'vertebrate,' 'mammalian,' or 'human' cDNA for insulin. Rutter disclosed the nucleotide and amino acid sequences of a rat cDNA encoding insulin, and described a general

procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat cDNA did not provide adequate descriptive support for the narrow subgenus of 'human' cDNA (no species disclosed), the larger subgenus of 'mammalian' cDNA (only the one rat species disclosed), and the larger genus of 'vertebrate' cDNA (only the one rat species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did acknowledge, however, the district court's statement that the specification provided adequate written descriptive support for the subgenus of 'rat' cDNA encoding insulin. *Id.* at 1566.

Thus, functional language should be acceptable when the genus as claimed is sufficiently limited in scope (i.e., from *Thermus*) and the specification describes one or more species within that genus. Claim 7 recites the same type of functional claim language that was identified as acceptable in *Eli Lilly* given the description of a single species by its nucleotide sequence. Thus, it should be evident that claim 7 (and claims dependent thereon) finds written descriptive support in the present application.

From all of the foregoing, it is apparent that one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the present application was filed. This is so, because persons of skill in the art would have expected sufficiently related thermophilic organisms from the genus *Thermus* to possess homologous *dnaX* nucleotide sequences or tau/gamma subunit proteins. McHenry together with Exhibits A-C confirm this expectation to have been reasonable.

In view of all of the foregoing, applicants submit that the rejection for lack of written descriptive support is improper and should be withdrawn.

The rejection of claims 7, 22, 28, 29, 81, 83-86, 88, and 89 under 35 U.S.C. § 112 (1st para.) as lacking enablement is respectfully traversed.

It is the position of the U.S. Patent and Trademark Office ("PTO") that the specification does not provide sufficient guidance in establishing regions of the protein structure which may be modified without effecting tau (or gamma) subunit activity, the general tolerance of the tau (or gamma) subunits to modification, and a rational and predictable scheme for modifying any amino acid residue of the tau (or gamma) subunit. Applicants respectfully disagree.

The PTO is respectfully reminded that all that is needed is objective enablement of what is claimed. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The present application provides the nucleotide sequence of *Thermus*

thermophilus dnaX (e.g., SEQ ID NOs: 1 and 3) and describes how one of ordinary skill can isolate homologs of the disclosed sequence (*see* page 34, line 7 to page 35, line 12; Example 1), express the tau (or gamma) subunits encoded by such homologous *dnaX* sequences (*see* Examples 2-6), and test the encoded tau (or gamma) subunit for activity (*see* Examples 6 and 8). Thus, one of ordinary skill in the art would have been fully able to make and use polynucleotides and proteins within the scope of the presently claimed invention.

Methods of identifying and producing variants of *T. thermophilus* Pol III γ and τ subunits have been practiced by those skilled in the art subsequent to the effective filing date of the present application. As addressed above, McHenry and attached Exhibits A-C identify three additional *dnaX* and tau/gamma homologs that share about 98% or greater homology at the nucleic acid level and about 97% or greater homology at the amino acid level. Each of the encoded tau/gamma subunits contains the ATP-binding and Zn^{2+} finger domains that are described in the specification. Thus, species of *dnaX* (encoding tau/gamma subunits) from thermophilic organisms that belong to the biological classification *Thermus* clearly share similar structure and, therefore, function.

For this reason, it is apparent that the present application fully enables the production of variants encoding the DNA-polymerase type-III τ and γ subunits of *T. thermophilus* as well as the production of polypeptide variants of the polymerase type-III τ and γ subunits of *Thermus* within the presently claimed homology range.

Therefore, the rejection under 35 U.S.C. § 112 (1st para.) for lack of enablement is improper and should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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